REMARKS / ARGUMENTS

Claims 21-47 are currently pending. The present Amendment amends claim 21. No new matter was added to this case by this Amendment. Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Amendments to the Claims and Support for Amendment

Independent claim 21 has been amended to more clearly specify that more than half of the lubricating agent is distributed on the tablet surface and the rest of it, if any, is included in the dry mixture. Support for this amendment can be found, for example, from page 1, line 32 to page 2, line 2 of the application, as originally filed.

Rejection under 35 U.S.C. § 103

The Examiner maintained the rejection of claims 21-39 and 40-41 under 35 USC § 103(a) as obvious over Hunter *et al.* (U.S. Pat. No. 6,391,337) in view of Schmidt *et al.* (U.S. Pat. No. 6,079,968), and Valentine (U.S. Pat. No. 4,684,534); and the rejection of claims 31 and 42-47 under 35 USC § 103(a) as obvious over Hunter *et al.* in view of Schmidt *et al.*

The Examiner did not find the arguments filed on May 3, 2008 to be persuasive. In particular, the Examiner stated that Hunter *et al.* teaches an embodiment wherein acetaminophen granules (of a size of 50-500 microns) are coated (Col. 13, lines 54-58) and that in this embodiment, the silicon dioxide is added to the acetaminophen granules and direct compression vehicle (*i.e.*, microcrystalline cellulose granules) and subject to shear mixing. The Examiner also stated that Hunter *et al.* teaches that the effect of mixing the silicon dioxide with the direct compression vehicle is that the vehicle is partially coated with the silicon dioxide (Col. 9, lines 9-21). The Examiner then concluded that in the embodiment wherein silicon dioxide is added to the acetaminophen granules, and subsequently mixed, it is reasonable that at least a portion of the granules are at least partially coated with the silicon dioxide, based on the substantially identical process using identical components.

Applicants respectfully disagree with this statement for at least the reasons set forth below.

In particular, Applicants submit that Hunter *et al.* teaches that in certain embodiments, the direct compression vehicle includes a microcrystalline cellulose (MCC) which has been ***coprocessed*** with silicon dioxide (SiO_2). This coprocessed direct compression vehicle is described as

> *an agglomerate of microcrystalline cellulose and silicon dioxide in which the microcrystalline cellulose and silicon dioxide are in intimate association with each other* [...]. *Magnifications of these coprocessed particles indicate that the silicon dioxide is integrated with, or partially coats, the surfaces of the microcrystalline cellulose particles*"

(see Col. 9, lines 12-22).

The Specification of the Hunter *et al.* patent does not provide a detailed description of methods that can be used to coprocess microcrystalline cellulose and silicon dioxide. However, a protocol to obtain a coprocessed microcrystalline cellulose is given in Example 1. In this protocol, microcrystalline cellulose in the form of a wet cake is combined with water in a mix tank to form a slurry. After adjustment of the pH with ammonium hydroxide, the slurry is allowed to mix for about 15 minutes before being combined with colloidal silicon dioxide. After allowing the materials to become intimately combined, the slurry is spray dried using a Niro Production Minor with an inlet temperature of 215°C, an outlet temperature of 125°C, and an atomizer wheel speed of 22,300 rpm.

Applicants also submit that Hunter *et al.* further teaches that silicon dioxide may also be present in the direct compressed pharmaceutical dosage form "*in an amount which is separate from and in addition to the silicon dioxide included with the coprocessed MCC (if used)*" (see Col. 10, lines 26-30). When silicon dioxide is a part of the pharmaceutical dosage form, "*it is preferred that the silicon dioxide be combined with the acetaminophen, direct compression vehicle and lubricant under the same* ***high shear conditions*** *used to create the homogenous mixture of the solid dosage form ingredients*" (see Col. 11, lines 43-51). Hunter *et al.* discloses

that "*the shear conditions under which the ingredients are combined can generally be described as a set of conditions* [...] *which permit the formation of the homogenous granulate but do not break down the materials undergoing the processing*" (see Col. 12, lines 19-24). Suitable apparatus for carrying out the high shear mixing taught by Hunter *et al.* include "*high speed mixers having an impeller or mixing blade* [...] *and a chopper or series of choppers* [...]" (see Col. 12, lines 28-33).

Thus, in embodiments where silicon dioxide is a part of the pharmaceutical dosage form described by Hunter *et al.*, silicon dioxide is ***high-shear mixed*** with the acetaminophen. The high-shear mixing undergone by silicon dioxide and acetaminophen is very different from the protocol (summarized above) used by Hunter *et al.* to obtain microcrystalline cellulose ***coprocessed*** with silicon dioxide. Therefore, Applicants submit that coprocessing and high-shear mixing are NOT substantially identical processes, as stated by the Examiner.

Furthermore, high-shear mixing and coprocessing do not lead to identical or substantially identical structures. Indeed, Hunter *et al.* indicates that high-shear mixing provides a "*homogenous granulate of the solid dosage form ingredients*" (see Col. 11, line 48), while coprocessing leads to the formation of particles where "*the microcrystalline cellulose and silicon dioxide are in intimate association with each other*" with "*the silicon dioxide* [being] *integrated with, or partially* [coating] *the surfaces of the microcrystalline cellulose particles*" (see Col. 9, lines 12-22). Hunter *et al.* does not teach or suggest that high-shear mixing results in coating or partial coating of acetaminophen granules with silicon dioxide. In addition, Hunter *et al.* does not teach or suggest that acetaminophen be coprocessed with silicon dioxide. Thus, it is NOT correct to conclude that, based on the substantial similarity of the processes (*i.e.*, high-shear mixing and coprocessing), when the silicon dioxide is mixed with acetaminophen granules at least a portion of the granules are at least partially coated with the silicon dioxide

Therefore, Applicants respectfully submit that in the tablet taught by Hunter *et al.* acetaminophen granules are NOT coated or partially coated (*i.e.*, are not covered with a layer of substance spread over their outer surface) with silicon dioxide. Applicants also submit that Hunter *et al.* does not teach or suggest a tablet comprising an active principle that is enveloped

by a coating, and more specifically an active principle that is in the form of coated microcrystals or coated microgranules, as recited in the present claims.

In light of the arguments put forward above, Applicants submit that Hunter *et al.*, taken alone or in combination with Schmidt *et al.*, and/or Valentine, do not teach or suggest all the limitations of the compressible tablet recited in independent claim 21, or of the process for making such a tablet as recited in independent claim 45, and therefore do not render obvious any claims of the instant application. Accordingly, Applicants respectfully request that the rejection be reconsidered or withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claim 41 under 35 USC § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner, stated that before the Amendment above, independent claim 21 required the lubricating agent to be both distributed on the tablet surface and mixed with the interior contents of the tablet. Dependent claim 41 requires all of the lubricating agent to be distributed on the table surface. The Examiner states that it is unclear how this limitation could fall under the scope of the the un-amended independent claim, since none of the lubricating agent would be mixed with the interior contents of the tablet. This was not the case with prior claim 21. It simply said that over half of the lubricaint agent be distributed on the tablet surface, clearly allowing for 100% of it to be there.

However, as mentioned above, claim 21 has been amended to specify that the tablet comprises a lubricating agent, wherein more than half of the lubricating agent is distributed on the tablet surface and the rest of it, if any, is included in the dry mixture. This amendment was made only to clarify things and to remove an issue that should not have been raised. This amendment was made not to narrow or otherwise change the scope of claim 21. The limitation of claim 41 clearly falls within the scope of independent claim 21 with or without the Amendment. The Amendment, however moots this rejection of claim 41.

Rejection under 35 U.S.C. § 102

Claims 21-25, 29-30, 33, 35 and 41 stand rejected under 35 U.S.C. § 102(b) as anticipated by U.S. Pat. No. 5,725,880 (hereafter the '880 patent or '880).

The Examiner stated that '880 discloses a plain tablet (a directly compressible tablet) comprising a dry mixture of 5-aminosalicylic acid (an active substance) and excipients including calcium carboxymethylcellulose (a disintegrating agent), calcium citrate (a soluble agent with binding properties), and magnesium stearate (a lubricating agent in power form), wherein more than half of the magnesium stearate is distributed on the tablet surface and wherein the active substance is in a form of coated microgranules (see Example 3). The Examiner acknowledged that the '880 patent does not disclose all the characteristics and properties of the composition recited the present claims, but states that he has reasonable basis to believe that the properties claimed in the present invention are inherent in the tablet disclosed by the reference based on the substantially identical process using identical components.

Applicants respectfully disagree, and submits that the '880 patent fails to teach every element of the claims rejected.

In particular, Applicants submit that '880 does not teach or even suggest a tablet comprising an active substance wherein the active substance is coated, let alone a tablet comprising an active substance, wherein the active substance is in the form of coated microcrystals or coated microgranules. The Examiner cites Example 3 as the basis for its statement that the active substance comprised in the tablet of the '880 patent can be in a form of coated microgranules. The tablet described in Example 3 is prepared as follows:

(a) The active substance (5-aminosalicylic acid) and corn starch are mixed together, and the mixture is granulated according to a wet granulation method using a binding solution of polyvinylpyrrolidone dissolved in ethanol. The obtained granules are dried and sieved to obtain granules for tabletting.

(b) The obtained granules, calcium citrate, calcium carboxymethylcellulose and magnesium stearate are then mixed together, and the mixture is tabletted by means of a rotary tabletting machine to obtain a plain tablet.

(c) The obtained plain tablet is then press-coated with a mixture of powder of hydroxypropylmethylcellulose acetate succinate, calcium stearate and magnesium stearate by means of a press-coating machine to obtain the final pharmaceutical preparation for oral administration.

Applicants submit that, as known in the art, the step of wet granulation (step a) does not result in the active substance being coated (*i.e.*, being covered with a layer of substance spread over its outer surface). Instead, the wet granulation provides substantially homogeneous granules of the solid ingredients (*i.e.*, 5-aminosalicylic acid, corn starch and polyvinylpyrrolidone). In such granules, the active substance may be considered as being trapped, dispersed, or embedded within a mixture of corn starch and polyvinylpyrrolidone; however the active substance is not coated.

It is axiomatic that a prior art reference must teach every element of a claim in order to anticipate that claim. The '880 patent fails to teach every element of the claims rejected by the Examiner. In particular, the '880 patent fails to teach or suggest a tablet comprising an active substance, wherein the active substance is in a form of coated microcrystals or coated microgranules. Therefore, the directly compressible tablets of claims 21-25, 29-30, 33, 35 and 41 are not anticipated by the '880 patent, and furthermore, could not be rendered obvious by the '880 patent.

As mentioned above, the Examiner stated that he has reasonable basis to believe that the properties claimed in the present invention are inherent in the tablet disclosed by the '880 patent based on the substantially identical process using identical components. Applicants would like to point out that the tablets claimed in the present Application are "adapted to disintegrate in the mouth on contact with saliva in less than 30 seconds," as recited in the claims. In contrast, the '880 patent describes a pharmaceutical preparation for oral administration from which a

medicinal active ingredient can be selectively delivered to any specific site in the intestinal tract. More specifically, the pharmaceutical preparation of the '880 patent

> "*has the following characteristics: when the pharmaceutical preparation is orally administered, the release of a medicinal active ingredient does not occur at all during residence of the pharmaceutical preparation in the stomach and, after discharge from the stomach, until the preparation reaches a desirable targeted site in the intestine and thereafter, the release of the ingredient starts rapidly*" (see Col. 2, lines 48-55).

Thus, the pharmaceutical preparation disclosed in '880 does not dissolve in the mouth. The "releasing" properties of the claimed compressible tablet and of the pharmaceutical composition disclosed in the '880 patent are entirely different. Therefore, it is unclear how the properties claimed in the present invention can be inherent in the pharmaceutical preparation of the '880 patent.

It is possible that Applicants misunderstood the argument and that the Examiner actually meant that the properties claimed in the present invention are inherent in the plain tablets disclosed in the '880 patent. If this is the case, then Applicants respectfully submit that the '880 patent fails to teach every element of the claims rejected.

In particular, Applicants submit that '880 does not teach or even suggest a tablet comprising a lubricating agent distributed on the tablet surface, let alone a tablet comprising a lubricating agent, wherein more than half of the lubricating agent is distributed on the tablet surface. Indeed, the plain tablets of the '880 patent are obtained through steps (a) and (b) mentioned above. The plain tablets of the '880 patent do not comprise the press-coated layer added in step (c). Therefore, the plain tablets do not comprise an additional amount of lubricating agent (magnesium stearate) distributed on its surface. Thus, the '880 patent fails to teach every element of the present claims. Therefore, the directly compressible tablets of claims 21-25, 29-30, 33, 35 and 41 are not anticipated by the '880 patent, and furthermore, could not be rendered obvious by the '880 patent.

In view of the arguments put forward above, Applicants request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

CONCLUSIONS

For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

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